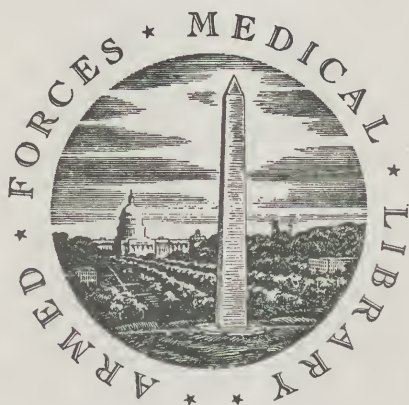




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A GAS-PRODUCING BACILLUS (*Bacillus Aerogenes Capsulatus*,  
Nov. Spec.) CAPABLE OF RAPID DEVELOPMENT  
IN THE BLOOD-VESSELS AFTER DEATH.

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## A GAS-PRODUCING BACILLUS (*Bacillus Aerogenes Capsulatus*, Nov. Spec.) CAPABLE OF RAPID DEVELOPMENT IN THE BLOOD-VESSELS AFTER DEATH.

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There are to be found in medical literature many cases in which the blood-vessels after death contained air or gas which did not seem attributable to post-mortem decomposition. Various explanations of this occurrence have been offered. The observation to be here reported is calculated to shed light upon some of these mysterious cases. The micro-organism to be described is in itself also of much interest.

The following is an abstract of the clinical history and post-mortem examination of the case.

J. M., male, light mulatto, aged 38, bricklayer. Admitted to the hospital, service of Dr. Osler, Oct. 24, 1890; discharged July 15, 1891; readmitted Oct. 24, 1891; died Oct. 25, 1891. Patient has used alcohol to excess and gives a history of syphilis. For two years has suffered from pain in the chest, dyspnœa, and paroxysmal cough. Spat blood three years ago. Six weeks before admission first noticed a pulsating lump on the right side of the chest. Upon admission there is observed a large, hemispherical, pulsating tumor in the right infraclavicular and mammary regions, reaching the border of the sternum, and most prominent in the second intercostal space. The skin over the tumor is intact and brownish in color. The manubrium sterni near the second costal cartilage is eroded. Percussion note over tumor is dull. Apex beat of heart in 5th interspace. No cardiac murmurs. Cardiac dullness not increased. No tracheal tugging. Arteries stiff, tension increased, pulse 84. No difference between radials. Pulmonary râles heard in scapular regions. While in the hospital the tumor gradually increased in size, extending from the sterno-clavicular articulation to the nipple, with complete erosion of sternum over about one-half its width. Thoracic and epigastric veins distended. Urine



free from albumen and casts. Patient left the hospital in July, 1891. When readmitted on October 24th, 1891, he reports that his condition remained about the same until a month ago, when a small ulcerated opening formed over the tumor, through which he lost about a pint of blood. A week later a larger rupture occurred on coughing, and he says that he lost about a gallon of blood, some coming through the mouth. A third hemorrhage occurred the night before readmission, when the blood spurted through both external openings, to the extent, he says, of about a gallon. Upon readmission the patient's condition did not appear to be immediately alarming. His mind was clear, appetite good, and there was no dyspnœa. The urine contained a small quantity of albumen with hyaline and granular casts. The patient died suddenly, without any further loss of blood, at 6 o'clock A. M., October 25th. In view of what was found at the autopsy, it may here be stated that no emphysematous swelling of the neck and no escape of gas from the ruptured openings of the aneurism were observed during the short time the patient lived after his re-entrance to the hospital, or immediately after his death, but no special attention was directed to these points.

The *post-mortem examination* was held eight hours after death, the weather being cool. The body was still warm and presented no discoloration of the skin of the abdomen or other signs of decomposition.

Rigor mortis present. Considerable emaciation. Puffiness of lower eyelids. Diffuse livid redness of face. Lower portion of neck up to the upper level of thyroid cartilage diffusely and symmetrically swollen, with emphysematous crackling, extending on the right side posteriorly to the vertebræ, on the left most evident anteriorly and laterally. Emphysematous crackling can be felt also in both axillæ, on the inner side of the arms, over the pectoral muscles, over the buttocks, in the groins and the inner side of the thighs. The subcutaneous veins over the abdomen and thorax, especially on the right side, are distended, tortuous, and contain gas-bubbles. Emphysematous crackling can be felt along the track of the superficial veins and over most of the body and extremities; it is limited to them.

Anteriorly on the right side of thorax is a tumor, with fluctuating feel, projecting about 4 cm. above the level of the skin, and extending from the first rib downward a distance of 12 cm., and laterally from the right margin of the sternum 11 cm., the most prominent part being 4 cm. from the sternal border. Near the most prominent part of the surface of the tumor are two circular openings through the skin, 1 cm. and 0.5 cm. in diameter, from which thin bloody fluid, mixed with gas-bubbles, escapes.

Before making the usual incisions into the abdomen and thorax, a number of veins and arteries, including the jugular, femoral and brachial veins, superficial veins of abdominal wall, femoral and temporal arteries, are carefully exposed by small suitable incisions

through the skin covering them, and the presence of gas-bubbles is determined in all of them without opening them. The presence of gas in the subcutaneous connective tissue of the neck is also determined by incision. The gas burns with a pale bluish, almost colorless flame, a slight explosive sound being heard at the moment of ignition.

Peritoneal cavity dry and not distended with gas. Visceral and parietal peritoneum, including omentum, studded with small, gray, translucent, firm nodules (miliary tubercles), averaging 0.5 to 1 mm. in diameter. Old fibrous adhesions around the spleen and between liver and diaphragm. Diaphragm on right side at 5th, on left at 6th rib.

Pleural cavities completely obliterated by old adhesions. Pericardial sac contains 30 cc. thin, blood-stained serum containing gas-bubbles. Dimensions of heart normal, save slight hypertrophy of right ventricle. Cardiac veins and arteries are full of gas. Right ventricle and auricle contain soft, dark-red coagula and thin, lac-colored blood, with which are mingled gas-bubbles in large number. The left cavities of the heart contain similar material in smaller quantity, together with gas-bubbles. Pulmonary artery and veins contain gas-bubbles. The muscular wall of the heart is soft and flabby and presents a peculiar spotted appearance on section. There are numerous small cavities, about 0.5 to 1 mm. in diameter, containing gas throughout the myocardium. Immediately around these cavities the muscular tissue has a pale whitish appearance. Cardiac valves normal, except a few whitish atheromatous patches on the aortic segment of the mitral valve. Thickness of wall of left ventricle 16 mm., of right ventricle 5 mm., length of ventricular cavity 7.5 cm., inner circumference of aorta just above valve 8 cm. Endocardium diffusely blood-stained.

Ascending arch of aorta much dilated, wall thickened, inner surface diffusely blood-stained and presenting many firm, partly calcified atheromatous patches. 5 cm. above the aortic valves, just above the duplicature of the pericardium, is a nearly circular opening 3.5 cm. in diameter, with sharply circumscribed, smooth, rounded edges in the anterior and right wall of the aorta. This opening, which is 2.5 cm. below the origin of the innominate artery, leads into a large aneurismal sac, which has developed chiefly forwards and to the right and produced the tumor visible externally. The aneurism measures 12 cm. in vertical and transverse diameters, and 7.5 cm. in antero-posterior diameter. It extends from the upper margin of the clavicle to the 4th rib. Its median border corresponds to the mid-line of the sternum. The eroded surfaces of the first, second and third ribs and of the sternum form a part of the anterior wall of the aneurism. The second rib has been completely destroyed at a point 3 cm. from the border of the sternum. The aneurismal sac is in relation above with the subclavian vein and innominate artery and vein, below with the pericardium, to the right with the upper lobe of the right lung, to which

it is firmly adherent, and on the median side with the thickened tissues of the anterior mediastinum. There are no evidences of pressure upon the œsophagus, trachea, or main bronchi. The walls of the aneurism are intact, except at the two openings in the skin already described. The sac of the aneurism is completely filled with coagula, those nearest the mouth being soft, dark-red post-mortem clots; the rest, which nearly fill the cavity, are laminated gray and reddish firm ante-mortem coagula, which can be removed with the fingers without much difficulty, except those nearest the wall, which are firmly adherent. The laminated coagula present pale white streaks and dots and contain many gas-bubbles.

Lungs, hyperæmic, œdematous, pigmented with coal; in upper lobes old cavities with fibrous wall and caseous contents, dense interlacing fibrous tissue, a few caseous nodules, and throughout both lungs many small, firm, gray miliary tubercles, without fresh pneumonia. Bronchi contain muco-pus, their inner surface diffusely reddened.

Spleen, dimensions 13 x 8 x 4 cm. Studded on its surface with miliary tubercles, with a few grayish tubercles in parenchyma, which is soft, brownish red, and on pressure permits a large number of gas-bubbles to escape. Malpighian bodies indistinct.

Kidneys, dimensions normal, capsule not adherent, surface smooth, thickness of cortex 8 mm. Markings coarse, color pale, a few small, grayish-yellow tubercles visible on the surface and on section. Gas-bubbles escape on section and by pressure from the renal blood-vessels. The tissues in the pelvis of kidneys are diffusely red, from imbibition of blood coloring matter.

In lower third of ileum are several scattered fresh tubercular ulcers, nearly circular in shape, not extending deeper than submucosa. Mesenteric glands pale, swollen, contain a few tubercles.

Stomach and duodenum contain much mucus. Dark, brownish-yellow bile can be readily squeezed from gall-bladder through common bile-duct.

Liver, dimensions 29 x 19 x 7 cm., presents emphysematous crackling on pressure. Surface and cut section present a peculiar mottled appearance, from the presence of many little, round, gas-containing cavities, about 1 to 2 mm. in diameter, which appear transparent as seen through the capsule. Walls of cavities appear smooth and formed by pale whitish liver substance. Hepatic parenchyma soft, pale and brownish in color. Gas-bubbles in large number in the vessels of the liver.

Urinary bladder contains 50 cc. clear urine. Flat, depressed scar on glans penis in place of frenum. Old scars in groins.

Aorta very atheromatous throughout its course. Large and small arteries present scattered patches of atheroma. The intima of all the large arteries and veins is diffusely red, from imbibition of blood coloring matter. The blood is thin, watery, transparent and lac-colored, and everywhere contains gas-bubbles. The gas-bubbles are both large and small. No distinct odor can be detected from



the blood, and in general there are no putrefactive odor and no greenish discoloration about the body.

*Microscopical examination of fresh blood and organs.*—The blood, taken with care from the interior of veins and arteries immediately after opening them, shows fewer and paler red blood corpuscles than normal. Many of the red corpuscles are irregular in shape, and there are shadows of corpuscles. There has evidently been a solution of some of the coloring matter of the red corpuscles. The leucocytes are swollen and their granules often in molecular movement.

The blood from the heart and vessels is rich in bacilli, about 3 to 5  $\mu$ . in length, about the thickness of anthrax bacilli, with ends slightly rounded, sometimes almost square-cut, occurring chiefly in pairs and in irregular masses and not in long chains. The same bacilli are present also in very large number in cover-slip preparations from the laminated clot of the aneurism, the liver, the spleen and the kidney. In all of these situations the bacilli appear to be in pure culture, no other species being observed. The bacilli are not motile. They stain readily with the usual aniline dyes, but often present small unstained spots. They possess a capsule, evident on the stained specimens.

Frozen sections of the fresh liver show the small cavities, visible to the naked eye, to be surrounded by liver cells, much disintegrated and fatty degenerated. Here the hepatic cells lie loose, with an indefinite granular detritus between them, whereas elsewhere the rows of liver cells, which also contain large and small oil globules, are preserved. Bacilli are present throughout the liver, but are by far most abundant in and near the small cavities. Several fresh miliary tubercles are seen in the sections.

Sections of the frozen fresh myocardium show also little cavities with many bacilli and disintegrating muscular fibers containing fine fatty granules in their walls. Elsewhere the muscular fibers show good striation, with a few scattered small oil globules. There appear to be more fatty granules in the broken-up fibers near the cavities than elsewhere.

Sections of the fresh kidney show with a low power areas darker and more opaque than the rest of the tissue and corresponding to groups of perhaps a dozen cortical tubules. In these areas the epithelial cells are finely fatty and desquamated, and here there are many bacilli, whereas elsewhere the epithelium does not appear much altered and bacilli are less numerous. A few small gas-containing cavities are present in the cortical substance. There are some atrophied glomeruli with thickened capsules, foci of increased intertubular tissue, thickened arteries, and many waxy casts in Henle's tubules.

*Microscopical examination of hardened organs.*—Small pieces of the organs were hardened in alcohol. Sections of these confirm the observations made on the fresh tissues. The liver shows many miliary tubercles with giant cells. These tubercles tend to become

fibrous rather than caseous. There is much bile pigment in the hepatic cells. There is a new growth of fibrous tissue in the external capsule of the liver. The interlobular connective tissue is moderately thickened, chiefly in irregular nodules and areas in connection with the tubercles. The kidney is the seat of chronic diffuse nephritis in moderate degree.

In the sections the bacilli stain readily with all of the ordinary aniline dyes (methylene-blue, gentian-violet, fuchsine) and stain well even with hæmatoxylin. They stain excellently by Gram's method, retaining the color after the nuclei have been decolorized. Their length averages one-half to two-thirds the diameter of the red blood corpuscles seen on the same sections, and their thickness is perhaps a little greater than that of anthrax bacilli, from which they are especially distinguished by not occurring in long chains.

The bacilli are found abundantly in the large arteries and veins throughout the lumen, but seem to be more numerous in the veins. Some sections of vessels, particularly of arteries, are free from the bacilli. Although some capillary blood-vessels are plugged full of bacilli or contain them in large number, most of the capillaries in the different organs do not contain them. The nuclei in the walls of the vessels containing bacilli, even those of the endothelium, stain well as a rule, but sometimes the nuclei do not stain. Occasionally the bacilli are found not only in the lumen but also in the walls of the vessels, and they occur in scattered spots in the tissues. The lymphatics in the pericardium are beautifully injected with masses of bacilli.

When the bacilli are accumulated in large masses in the tissues the surrounding nuclei usually do not stain. These bacillar masses can be seen with the naked eye on stained specimens as deeply stained dots, and occur scattered irregularly. The zone of unstained nuclei around the clumps of bacilli in the tissues is wider in the liver than in the kidney, and wider in the kidney than in the heart muscle. Elsewhere the nuclei stain well. The absence of nuclear staining must be due to the products of the growth of the bacilli, for it occurs at a considerable distance, for instance the thickness of a lobule in the liver, from the spot where the bacilli are present. There is no nuclear fragmentation. The nuclei either cannot be made out at all or appear as very pale bodies. In the heart muscle near the masses of bacilli in the tissue the nuclei seem smaller than elsewhere, whereas in the liver there are many nuclei swollen to three or four times their normal size, appearing as empty cavities with a stained rim, suggesting somewhat drops of fat, from which, however, they can be readily distinguished by the sharp stained ring around them and the transitions to the normal nuclei. These peculiarly altered nuclei can be seen scattered irregularly through the liver as well as in or near the areas with unstained nuclei. There is absolutely no evidence of reaction in the tissues around these areas or the masses of bacilli.

The cavities which were visible to the naked eye and on frozen



sections as gas-blebs appear on the hardened sections. They vary in size and shape. The smaller ones are regularly round, often with smooth walls. Larger ones, which may be 1 to 2 mm. in diameter, may be oval or irregular in shape, and evidently may be formed by the coalescence of smaller cavities. The bacilli are in almost or quite continuous mass in the margin of these cavities, and for a variable distance around them the nuclei do not stain. There is evidence of pressure upon the tissues around the cavities. Areas can be seen in which dense masses of bacilli lie between the broken-up loose tissue elements (liver cells, muscle-fibers) without stained nuclei. In spots in the liver the intralobular capillaries are plugged with bacilli. Exceptionally, bacilli are present in the lumen of urinary tubules. They are generally absent from the intertubular and glomerular capillaries, and are more abundant in the cortex than in the pyramids. The bacilli are much more numerous in the hepatic and portal veins than in the hepatic arteries.

*Cultures* in nutrient agar-agar were made from the heart's blood, the aneurismal clots, the liver, spleen and kidney. These cultures were made according to our usual custom in the progress of the autopsy. The surface of each organ as soon as exposed is thoroughly burnt over a sufficient area by a flat piece of metal heated to redness, and Nuttall's thick platinum needle<sup>1</sup> thrust into the interior through the burnt area. As it seemed probable that the bacilli found on the cover-slips would prove to be anaerobic, in addition to the ordinary roll cultures, tubes one-half or three-quarters filled with liquefied agar at 40° C. were inoculated with material from the platinum loop, and after thorough mixing the agar was allowed to solidify in the upright tubes. The tubes were placed in the thermostat at 37° C.

After 24 hours no growth appeared in any of the roll cultures and none subsequently developed. On the other hand the tubes of high agar showed an abundant growth in the form of small, grayish-white colonies, with many gas-bubbles, in the lower two-thirds of the agar, but no growth in the upper third. The organism in the cultures is therefore anaerobic and incapable of development in plain agar in the presence of much free oxygen. Microscopical examination of the cultures showed only one species, and that a bacillus identical morphologically with that found in the cover-slip preparations of the fresh blood and organs. The cultures from the blood and

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<sup>1</sup> Nuttall. Centralblatt f. Bakteriologie, 1892, Bd. XI., No. 17, p. 538.

all the organs mentioned presented the same appearance and were pure of this same bacillus. From single colonies other tubes of high agar were inoculated, and thus the organism was obtained in pure culture for further study, the results of which will now be presented.

*Morphology.*—The usual form of the bacillus is straight, but sometimes in fresh cultures, more frequently in old ones, slightly curved or bent forms are seen. The ends of the bacillus are slightly rounded, or they may appear, especially the adjacent ends in pairs or short chains, as nearly or quite square-cut, but this latter appearance is not so uniform and outspoken as with the anthrax bacilli.

The bacillus varies somewhat in size, especially in length, in different culture media. It appears usually thicker and more variable in length in artificial cultures than in the blood of animals or of man. The average thickness in fresh cultures is a little greater than that of the anthrax bacillus. The average length in fresh cultures may be placed as 3 to 6  $\mu$ ., but forms are common in the same culture which are shorter, as well as those which are two to three times longer.

The bacilli occur singly, in pairs, in clumps, and sometimes in short chains. When placed end to end the rods may be in a straight line, but they are often at an angle with each other. Long chains and long threads have been seen exceptionally both in the blood of animals and in cultures, but the absence of a tendency to grow in long chains is a distinguishing point between these bacilli and those of anthrax.

The bacillus is not motile. This point has been tested repeatedly both in the blood of animals and in fresh bouillon and agar cultures.

As has already been mentioned for the sections, the bacilli stain readily with ordinary aniline dyes. With Gram's method the dried and heated cover-glass preparations do not retain the dye so persistently as do the sections of alcohol-hardened specimens. With methylene-blue the rods from fresh cultures stain uniformly, or they may show little unstained dots irregularly placed and occasionally so numerous as to give a granular or vacuolated appearance to the rods. Less frequently are also seen in some bacilli specks more deeply stained than the rest of the rod.

Capsules can often be demonstrated around the bacilli, but they do not seem to be constantly present. They make one of

the most important morphological features of the bacillus. They have been found both in cultures and in the animal body. They appear as clear zones when unstained. We have found the following method well adapted for bringing to view the capsules, which, however, may appear by ordinary methods of staining. The dried and not overheated cover-slip preparations are treated first with glacial acetic acid, which is allowed to drain off and is at once replaced by a strong aqueous solution of gentian-violet, which is to be added several times until it has taken the place of the acid. The specimen is then examined in the coloring solution, the thin layer of which left under the cover-glass after soaking up the excess with filter-paper not interfering with a clear field. The capsules are then very distinct, but often not in water or after mounting in balsam. The width of the capsule varies from one-half to twice the thickness of the bacillus, these differences depending on the exact method of treatment as well as on actual differences in thickness. The outer margin of the capsule is stained, leaving as a rule a clear zone immediately around the bacilli. We have been most successful in demonstrating the capsules in cultures in plain agar and in the blood of rabbits.

Various involution forms are found in old cultures. The most remarkable ones were observed in five per cent and ten per cent sugar gelatine cultures a month old. Here we observed long threads, sometimes reaching through several fields of the microscope (homogeneous immersion  $\frac{1}{12}$ ), thin rods, thick rods, irregularly swollen, varicose rods, pear-shaped rods, exquisite spiral forms, curved and bent forms, rods with distinct capsules without special staining, and various irregularities in staining. Fresh cultures from these old ones were pure of the typical bacilli. In an agar culture four months old we observed also remarkable involution shapes, including some very small, coccus-like forms and capsules containing small stained particles or even empty. On the other hand a sugar bouillon culture of the same age was nearly free from involution forms, and a sealed tube containing an agar culture 89 days old was also nearly devoid of unusual forms.

The bacillus does not form spores.

*Cultures.*—The bacillus is capable of growth upon all of the ordinary culture media. It grows best at temperatures of 35°–37° C., but it grows also at ordinary room temperatures

(18°–20° C.). It is anaerobic. No growth takes place in plain or in sugar bouillon without removing the oxygen. In solid media, gelatine and agar, inoculated as soon as solidified after thorough steaming, it grows in the deeper layers even when the air has free access to the tube. For making anaerobic cultures various procedures were adopted, but the one found most convenient, and which we used chiefly, was to place the tubes in narrow cylindrical jars (a little higher than the length of the test tubes) containing pyrogallic acid and ten per cent caustic potash solution, according to the method recommended by Buchner.<sup>1</sup> Although the oxygen is not as completely displaced by this method as by some others, it is sufficiently absorbed for our purpose. The stopper of the jar was sealed with a thick layer of paraffin.

*Cultures in nutrient agar-agar.*—Gelatine and agar tubes were usually inoculated as soon as the medium was solidified after thorough steaming by which the air is temporarily displaced. For cultures in high agar or gelatine the tubes were filled one-third to one-half of their height with the medium. Stab cultures were made with a long platinum needle reaching to the bottom of the tube.

These cultures in ordinary neutral or alkaline nutrient agar to which the air has free access through the cotton plug show a good growth at the end of 24 hours at body temperature. The colonies in the lower part of the needle track are larger than those above, the uppermost ones being very minute. The growth reaches to a variable height beneath the surface. It usually ceases about 10 to 12 mm. below the surface when the tube has been inoculated after sufficiently prolonged steaming to displace all of the air. In other cases it may not come within 3 to 4 cm. of the surface. After artificial cultivation for several generations the growth seems to approach nearer the surface than at first. The colonies are grayish white to a more opaque white or even brownish white color by transmitted light, sometimes with a central darker dot, the opacity of the color depending upon the thickness of the colony. The largest colonies at the end of 24 hours do not exceed 0.5 to 1 mm. in diameter. They may subsequently attain a diameter of 2 to 3 mm. or even larger. They appear as spheres or ovals, generally more or less flattened, with usually

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<sup>1</sup> Buchner. Centralblatt f. Bakteriologie, 1888, Bd. IV., p. 149.

irregular contours, the irregularity being due to little projections or prongs from the surface of the colonies, these irregularities being more evident with a loop than with the naked eye. The colonies may appear as little irregular masses with projections. After several days or weeks, single, well separated colonies may attain a large size and be surrounded with projections either in the form of little knobs or spikes or of fine branching hair-like or feathery processes. In the former case the colonies present a mulberry or thornapple appearance; in the latter they may be compared to spherical white thistle-balls or powder-puffs. Such colonies in old cultures sometimes reach one cm. in diameter. Similar feathery projections may be present in places when the stab growth is continuous.

Bubbles of gas make their appearance in plain agar as well as in sugar agar, although less abundantly in the former, and sometimes not appearing until after 24 hours. These bubbles first appear in the line of growth, but they are soon present throughout the agar, often at a distance from the actual growth. Fluid is pressed out into the spaces occupied by the bubbles as well as upon the surface of the agar, and this fluid may be turbid from the presence of bacilli. The production of gas is less abundant at room temperatures than at that of the thermostat ( $35^{\circ}$ – $37^{\circ}$  C.) There is usually no very distinctive odor to be appreciated from the cultures in gelatine or agar, but there is an odor, not easily described, not putrescent, something like that of stale glue, and this odor is in some cultures more pronounced than in others. It was sometimes noticed that when the agar cultures were thoroughly crushed in a little bouillon a foul odor can be detected.

Nutrient agar containing one per cent glucose permits a much more rapid and luxuriant growth and especially more abundant and speedy gas-formation than does plain nutrient agar. Here the growth in high layer comes nearer the surface, often within 2 to 3 mm. when the air has free access to the tube through the cotton plug. Neutral or slightly alkaline media were employed, and these were turned strongly acid by the growth of the bacillus. In anaerobic cultures in sugar agar made according to Buchner's method the production of gas is so great as often to split the agar and force it into the upper part of the tube. In these anaerobic cultures there is of course less difference between the size of the colonies in the lower and those in upper layers, and the growth usually comes



to the surface, but does not spread out there. Generally an excessive quantity of fluid accumulates on the surface, and this is turbid from the presence of the bacilli. The agar is not liquefied by the growth of the bacilli.

*Cultures in nutrient gelatine.*—The bacillus grows in ordinary neutral or alkaline nutrient gelatine, but not so well as in that containing glucose. Gas is formed in both media, but much more abundantly in sugar gelatine. 5 per cent gelatine is much better than 10 per cent gelatine for the development of the bacillus. The bacillus is best classed among the non-liquefiers of gelatine, although in anaerobic cultures in 5 per cent sugar gelatine there may be slight softening due to peptonization of the gelatine over a limited area, as is made manifest by the settling of the growth toward the bottom of the line of puncture in stab cultures, and by slight displacement of the gas-bubbles in changing the position of the tube. Cultures in gelatine which have developed at 35°–37° C. become solid upon cooling the tube. In gelatine cultures at 20°–23° C. in high layer to which the air has free access through the cotton plug, the growth occupies the lower third to one-half of the medium, not reaching as near the surface as in agar cultures at body temperature. The appearance of the colonies in gelatine does not differ especially from that of those in agar.

*Cultures in bouillon.*—We have not noticed any development of the organisms in tubes of bouillon to which the air has free access, but the growth is abundant in anaerobic cultures in both plain and sugar bouillon. In sugar bouillon there is very abundant gas-formation, small bubbles accumulating on the surface so as to form often a foamy layer. As soon as the development of the organism begins it goes on with extreme rapidity, so that clear bouillon may become very cloudy with an abundant sediment in two or three hours. The development in sugar bouillon is well marked in Buchner's jars in less than 18 hours. The diffuse cloudiness of the bouillon gives place to a clearer or even an absolutely clear and transparent appearance in the course of a few days by the settling of the sediment. This sediment is abundant, white, uniform or sometimes flaky. Upon shaking it floats up in viscid threads or clouds or, if in flakes, can be readily broken up so as to mingle uniformly with the fluid and produce diffuse cloudiness, or it may be in the form of little specks less easily disinte-

grated by shaking and quickly settling again upon standing. The reaction of the sugar bouillon is of course strongly acid after the development is completed. The odor of bouillon cultures is like that of agar cultures and may be compared to sour stale glue. It is not a distinctly putrescent odor.

*Cultures in milk.*—Growth is speedy and abundant in anaerobic milk tubes at body temperature, but was not observed in tubes exposed to the air. In 24 to 48 hours the milk is coagulated, the clot being either uniform or firm, retracted and furrowed with the marks of gas-bubbles which develop abundantly. In milk colored with blue litmus, which is of course completely decolorized simply by absorption of oxygen in anaerobic cultures, the coagulated milk becomes deep pink upon exposure to the air.

*Cultures upon potato.*—In potato tubes prepared according to Bolton's method<sup>1</sup> and put in the Buchner jars and kept at body temperature, abundant gas-formation occurs in 24 hours in the fluid accumulated around the bottom and sides of the potato, which thus becomes surrounded with a frothy fluid. After complete absorption of the oxygen there appears a thin, moist, grayish-white growth on the surface of the potato.

The bacillus grows well with formation of gas-bubbles in ascitic fluid in anaerobic culture.

*Vitality.*—As already mentioned, the bacillus forms no spores. The vitality of the cultures is of very variable duration, according to the character of the medium and the mode of cultivation. Cultures in sugar bouillon in Liborius tubes in which the oxygen was replaced by hydrogen we found to be dead in three days and they may die sooner. On the other hand we found a sugar bouillon culture kept for 123 days in Buchner's jar at body temperature to be still living. The same was true of a culture in plain agar. Cultures in sugar agar are shorter-lived than those in plain agar and may be dead in 28 days or even less. A culture in plain agar exposed all of the time to the free entrance of air through the cotton stopper had a few living bacilli at the end of 84 days, although most of the organisms were dead. Cultures in sugar gelatine appear to be longer-lived than those in sugar agar, and cultures kept in Buchner's jar longer-lived than those to which the air can enter. There were curious and not readily

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<sup>1</sup> Bolton. The Medical News, 1887, Vol. I., p. 318.

explained differences in the vitality of the cultures, some being still alive which were under apparently the same conditions and of the same age as those which proved to be dead. A convenient way of keeping the cultures alive for a long time is to seal the agar tubes hermetically after two or three days' growth.

*Thermal death-point.*—This was tested according to Sternberg's method<sup>1</sup> on fresh bouillon cultures. These were killed by exposure for ten minutes to a temperature of 58° C. They were not completely killed by the same temperature after five minutes.

*Inoculation of animals.*—Quantities up to two and one-half cubic centimeters of fresh cultures in sugar bouillon and of suspensions in salt solution or bouillon of fresh agar cultures were inoculated into the ear veins of rabbits without any manifest symptoms, the animals surviving. Larger quantities were not employed. In only one instance was a rabbit killed by intravenous inoculation, and this case will be described later. We cannot therefore consider this bacillus as pathogenic for healthy rabbits under ordinary conditions.

If, however, the animal be killed after the intravenous injection of the bacilli, then these develop in the vessels, tissues and organs with abundant formation of gas. Upon this point we have made twenty experiments upon rabbits and one upon a dog. The animals were killed at a variable period after the injection. As the results of these experiments were uniform and conclusive, it is necessary to give only a few of the protocols as examples.

*Experiment 1.*—Large rabbit. 1 cc. sugar bouillon culture (the ninth generation from the original case) 24 hours old, which had developed in Buchner's jar at 36° C., showing abundant growth with gas production, was injected into the ear vein and immediately after the injection the rabbit was killed by a sharp blow at the back of the neck. The animal was kept in a room the temperature of which was about 18°-20° C. A control rabbit was killed and kept under the same conditions. At the end of 18 hours emphysematous crackling could be felt in the groins of the inoculated rabbit and elsewhere. The femoral vessels were now exposed and found to be full of gas-bubbles. The autopsy was then made. Peritoneal cavity full of gas. The heart cavities contain soft, dark coagula with lac-colored blood and many gas-bubbles. The blood-vessels, both arteries and veins, are full of gas-bubbles. The

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<sup>1</sup>Sternberg. Am. Journ. of the Med. Sciences, July, 1887, p. 146.



abdominal vena cava and other abdominal veins are blown up with a continuous volume of gas. The inner coat of the blood-vessels is diffusely red from imbibition of blood coloring matter. The liver is soft, pale and crackling. It is studded with little cavities containing gas. The spleen is soft, crackling and swollen with gas-bubbles. The kidney also contains gas. The tissues around the kidney, the retro-peritoneal tissue, the tissues in the groin, over the abdomen, are emphysematous. The gas burns with a bluish flame, and upon ignition a slight explosive sound is heard. Blood-stained fluid in the pericardium and pleura contains gas-bubbles. No odor of putrefaction. Cover-slip preparations from the blood-vessels, liver and spleen show an enormous number of bacilli, like those injected, provided with beautiful capsules easily demonstrable by the acetic acid method. No other species of bacteria are observed. Anaerobic cultures and cultures in high liquefied agar from the blood and spleen prove to be pure cultures of the typical bacilli.

The control rabbit shows no development of gas in the vessels or organs. No bacteria are found in the blood, and cultures from the blood are negative.

*Experiment 2.*—Full-grown rabbit. 0.5 cc. 24-hour anaerobic sugar bouillon culture (13th generation) into ear vein. Killed after 5 minutes. Kept for 24 hours under same conditions as the preceding rabbit. At the end of this period animal much swollen, abdomen distended and tense, emphysematous crackling of subcutaneous tissues. Gas abundant in heart and blood-vessels, serous cavities, spleen, liver and other parts. Bacilli present in large number. Cultures from heart's blood pure of the typical bacilli. Control rabbit free from gas formation in vessels.

*Experiment 3.*—Large rabbit. 1 cc. of the same culture as that used for preceding rabbit injected into ear vein. Killed after one hour. The inoculated ear cut off near the base and remaining cut surface burnt. Result as in preceding case, but animal not so much swollen from gas formation.

When the animal is killed shortly after the injection into the circulation and is then kept at temperatures between 30° and 35° C. the development of bacilli and gas goes on with almost startling rapidity, as is illustrated by the following cases:

*Experiment 4.*—Medium-sized rabbit. 1 cc. anaerobic sugar bouillon culture (17th generation), 24 hours old, into ear vein. Killed after two minutes and immediately placed in incubator regulated accurately at 32° C. Autopsy made 6 hours after death. Abdomen much distended. Emphysematous crackling over thorax, abdomen and inside of thighs. On incision, gas, which burns with a blue flame, escapes freely from the abdominal cavity. Fundus of stomach digested. Vena cava inferior and other abdominal veins appear to contain no blood, but to be blown up with a continuous

volume of gas. Abdominal aorta contains gas-bubbles and a little blood, but is not distended. The heart cavities and blood-vessels everywhere contain gas. The liver is completely filled with small and larger gas-bubbles, forming a pale, soft emphysematous pulpy mass. Many of the gas-blebs at the surface have ruptured. Spleen full of gas-blebs. Gas in kidney. Muscles of thigh and elsewhere streaked with whitish lines containing gas. Pleural and pericardial sacs full of gas. Emphysema of sub-pleural and sub-peritoneal tissue. Urinary bladder free from gas. Blood lac-colored, with soft dark clots. Typical capsule-staining bacilli in enormous number in the blood, liver, etc. No other species observed. Cultures from the blood are pure of the bacillus injected.

A control rabbit killed at the same time and kept in the incubator was examined after 8½ hours. It presented beginning greenish discoloration of the abdominal walls. No gas in the heart, blood-vessels, liver or serous cavities. A few bacteria in the portal vein, none found elsewhere in the blood. Cultures from the blood and organs sterile.

This case shows that in the short space of 6 hours after death gas and bacilli have developed at the temperature of 32° C. enormously, and to a greater degree than is observed after 24 hours at ordinary room temperatures.

*Experiment 5.*—Large rabbit. 1 cc. anaerobic sugar bouillon culture (19th generation), 48 hours old, into ear vein. Killed after one minute by blow at back of neck, kept in incubator at 30° C. Examined after four hours. No subcutaneous emphysema. Gas-bubbles in femoral vessels. Gas and frothy reddish serum in moderate amount in peritoneal cavity. Stomach not digested. Vena cava abdominalis distended with large gas-bubbles mixed with dark blood. Smaller gas-bubbles in abdominal aorta. Arteries and veins generally contain gas. Gas more abundant in right than in left cavities of heart, in pulmonary artery than in pulmonary veins. Liver contains many gas-blebs. Gall-bladder distended with gas. Gas-blebs in spleen, gas in pleural cavities, in diaphragm, in sub-serous tissues. Blood shows under microscope distorted and pale red blood corpuscles, yellow plasma and leucocytes swollen, presenting molecular movement of granules and round apparently empty nuclei. Typical bacilli in pure culture in blood and elsewhere.

This case shows that at the temperature of 30° C. the bacilli and gas have developed to a marked degree within 4 hours after death, the animal having been killed one minute after intravenous injection of 1 cc. bouillon culture. The dead animal body evidently offers the most favorable conditions possible for the growth of the bacillus. This growth

is many times more rapid at warm temperatures than at temperatures below 20° C.

Several experiments were made to determine the difference in time required for the development of the bacilli with formation of gas throughout the blood-vessels when the organisms are introduced only at one point in the vascular system after death and when they are distributed, as in the preceding experiments, just before death throughout the circulation.

*Experiment 6.*—Large rabbit. Killed by chloroform. Four hours after death a small window was cut in the thorax, the surface of the left ventricle singed with a hot knife, and two loopfuls from a 72-hour anaerobic agar culture (7th generation) thrust into the left ventricle. The rabbit was kept in the room at a temperature of 18° to 20° C. After 24 hours the femoral vessels were exposed and found to be free from gas. After 48 hours gas was found in the femoral artery, but none in the vein. The autopsy was then made. Gas-bubbles quite abundant in all of the arteries, also in both sides of the heart, pulmonary vein, pulmonary artery and venæ cavæ near the heart, but none was found in the veins elsewhere, and none in the liver, spleen or connective tissue. Cover-slip preparations from the heart and aorta show the characteristic capsulated bacilli in large number, but no bacilli are found in the abdominal vena cava, the femoral vein or the liver. Cultures from the blood in the thoracic aorta are pure of the same bacillus, those from the abdominal vena cava are sterile.

In this case, therefore, at room temperature the bacilli after 48 hours had not made their way into the veins except those near the heart, but had grown throughout the arteries; whereas after 18 hours in experiment 1, in which the bacilli had been introduced into the circulation just before death and the rabbit had been kept under the same conditions, all of the vessels and organs and serous cavities were full of gas and bacilli.

In the following experiment the culture was introduced into the right ventricle shortly after death and the animal was kept at the temperature of 32° C.

*Experiment 7.*—Rabbit killed by blow at back of neck. One-half hour after death heart exposed, and after singeing the surface, 0.5 cc. of the same sugar bouillon culture as that used in experiment 4 injected with fine hypodermic needle into right ventricle, no air being permitted to enter. This rabbit was kept together with that of experiment 4 and a control rabbit in the incubator at 32° C. and was examined after 7½ hours. No subcutaneous emphysema. No

gas in femoral artery or vein. No gas in peritoneal cavity, liver, spleen or kidney. Stomach not digested. Gas-bubbles in abdominal vena cava, renal, portal, hepatic veins, in veins near the heart, in both sides of heart, pulmonary artery, pulmonary veins and thoracic aorta, none in abdominal aorta. The gas is most abundant in vessels leading to or from the right heart, and is in comparatively small amount in the vena cava in the abdomen. Cover-slip preparations show numerous typical bacilli in pure culture wherever gas is present. The bacilli are abundant in a smear preparation from surface of lung. None are found in the abdominal aorta. (The control rabbit of experiment 4 served also as the control for this experiment.)

If the result of this experiment be compared with that of experiments 4 and 5 in which the autopsies were made after 6 and 4 hours respectively, it is evident that it requires a much longer time even at high temperatures for the bacilli and gas to develop throughout the vessels and organs when they are introduced at one point after death than when they have been distributed throughout the circulation just before death, a result which of course might have been predicted.

The last two experiments are also interesting as showing that the bacilli first grow in the course of the circulatory channels into which they have been introduced, in experiment 6 along the arteries and in experiment 7 along the veins, and in both cases through the pulmonary circulation.

Of all of the organs of the body the liver appears to offer the most favorable conditions for the rapid development of the bacillus after death and the formation of gas. Some of our observations seem to indicate that the bacilli develop sooner in the veins than in the arteries, but our attention was not directed sufficiently to this point to justify a more positive statement.

The length of time that the bacilli injected into the circulation may survive in the living body we have not accurately determined, but they may persist for at least 48 hours and probably longer. It requires a longer time for the bacilli and gas to appear throughout the vessels when the animal is killed several hours up to two days after the injection than when it is killed immediately. These points are shown by the following experiment.

*Experiment 8.*—Large rabbit. 1 cc. 48-hour sugar bouillon culture (16th generation) in ear vein. Killed after 48 hours by blow on back of neck. Kept for five hours at temperature of 32° C. and

then at temperature of 20° C. Autopsy after 32 hours. Animal enormously swollen. Subcutaneous emphysema. Abdomen distended with gas. Vessels and liver full of gas. Enormous number of typical bacilli in blood and organs. Cultures from blood pure of the characteristic bacilli.

Out of six experiments upon rabbits to determine the pathogenic effects of the bacillus, only one died from the effects of the inoculation, and this afforded an interesting result.

*Experiment 9.*—Pregnant rabbit. 1 cc. sugar bouillon culture (9th generation), 48 hours old, into ear vein. Rabbit was found dead 21 hours after the inoculation, the body being still warm, although stiff. It was alive one-half hour previously and apparently in good condition. The autopsy was made 6 hours after death. By this time the body, which has been in a room at the temperature of about 18° C., is much swollen, the abdomen distended, and emphysematous crackling can be felt over the abdomen and the lower part of the thorax. Bloody fluid containing gas-bubbles oozes from the vagina. On opening peritoneal cavity gas escapes freely, which burns with a colorless flame, a slight explosive sound being heard upon first applying the match. This cavity contains blood-stained fluid. Blood-vessels, both veins and arteries, contain gas. The heart cavities on both sides contain soft dark clots with gas-bubbles. Spleen is somewhat enlarged, soft and dark red. Liver does not contain gas-blebs, but gas is present in hepatic vessels. The inferior vena cava is blown up with gas. The uterus contains 6 embryos about 3 cm. long. The dilatations of the uterus corresponding to these embryos are greatly distended with gas. Two of the sacs are more distended than the rest, their walls are very thin, contain gas-bubbles, and look as if they were just ready to burst. The embryos in these two sacs are macerated, dark livid red, partly destroyed and smaller than the rest, which are intact. The placentæ contain gas-bubbles in large amount.

Cover-slip preparations show an enormous number of characteristic capsulated bacilli in the distended uterine sacs, a large but not so great number in the liver, spleen, heart and blood-vessels. Cultures from the uterus, spleen and left ventricle are pure of the typical gas-forming bacillus which was used for the injection.

The preceding case is instructive as showing that under special conditions the injection of cultures of the gas bacillus may prove fatal. The special condition existing in this rabbit and not in any of the others used for these experiments was pregnancy. It seems probable from the autopsy that two of the embryos in the uterus were already dead when the injection was made, and that in these embryos and the part of the uterus containing them the bacilli were able to gain a foothold and develop.



The case is especially suggestive in view of the number of cases which have been reported of death from supposed entrance of air into the uterine veins after abortions and injections into the uterine cavity. It will be noted that the autopsy was made in six hours after the death of the animal, and that already the vessels and peritoneal cavity were full of gas and that there was subcutaneous emphysema, a condition not found when the animal is killed immediately after the injection of the cultures, kept at room temperature, and examined at that short period after death.

*Conclusions from the experiments.*— Our experiments, although they have not settled all of the points which suggest themselves as to the relation between our gas-producing bacillus and the animal body, have settled the principal questions which we had in mind when we began the experiments. We may draw the following conclusions from these experiments on animals.

The bacillus is not pathogenic under ordinary conditions for healthy rabbits in doses up to 2.5 cc. of fresh bouillon cultures. Doses of one cubic centimeter may, however, under especial conditions, prove fatal, the special condition in our experiment being pregnancy probably associated with the death of two embryos either before or soon after the injection.

The bacillus develops rapidly in the blood after death, with formation of gas.

If the animal be killed immediately or soon after the intravenous injection of 0.5 to 1 cc. bouillon culture, after 18 to 24 hours at the temperature of 18°–20° C. and after 4 to 6 hours at temperatures from 30° to 35° C. the bacilli are found abundantly, together with great formation of gas in the blood-vessels and organs.

When the animal is killed several hours up to two days after the intravenous injection it takes a longer time before the bacilli develop throughout the vessels and tissues with gas formation, than when the animal is killed at once after the injection.

When the bacilli are introduced at one place in the vascular system soon after death, they develop in the course of the vessels into which they are introduced, and the time required for them to appear with gas formation throughout the vessels is at least two or three times as long as when the bacilli have been distributed throughout the circulation just before death.

It is noteworthy that in the instance in which the pregnant rabbit died from the effects of the inoculation death was sudden, and that within six hours after death the vessels contained gas and bacilli in large amount.

All of the conditions relating to the bacilli and their production of gas which existed at the post-mortem examination of the patient J. M. were produced experimentally in animals by inoculation of pure cultures of the bacillus isolated from the body of the patient.

It is our intention to continue the experiments in order to determine more accurately how long the bacilli may survive in the body of a living animal, how they are disposed of there, and the possibilities of their exerting pathogenic effects under certain circumstances.

In endeavoring to select a name suitable for the bacillus described in this article we have thought of several designations, such as the following: *Bacillus aerogenes capsulatus*, *bacillus sanguinis aerogenes*, *bacillus aerogenes cadaveris*, *bacillus pneumathæmiæ*. (The name *pneumathæmia* was introduced by Cless to designate the presence of air in the blood.) Upon the whole we prefer the first name, *bacillus aerogenes capsulatus*. The presence of a capsule does not appear to be constant, but it is common and forms a characteristic feature of the morphology of the bacillus.

We have not been able to identify the bacillus with any hitherto described, but the descriptions of some of the gas-producing bacilli have been so meagre and unsatisfactory that it is possible that others have found the same organism. We find indeed records in our laboratory notes of encountering from various sources obligatory anaerobic gas-producing non-motile bacilli, some of which may have been identical with the present one, but these organisms were not studied sufficiently to establish their identity and the cultures have not been kept. There is a note of finding such a bacillus in the human lung at autopsy, but there was no gas production in the body. We think it likely that our *bacillus aerogenes capsulatus* is not an uncommon species. The bacillus described by E. Fränkel<sup>1</sup> in a case of gastritis emphysematosa may have been identical with ours, but it was studied only on hardened specimens of the stomach. There may of course also be other bacteria capable of producing similar effects in the animal body.

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<sup>1</sup> E. Fränkel. Virchow's Archiv, Bd. 118, p. 526, 1889.

We will now review briefly the main points in the case which formed the starting point of our investigations, and consider the bearing of the case upon other similar ones recorded in medical literature.

A patient with chronic pulmonary tuberculosis, acute miliary tuberculosis and a large sacculated aneurism of the ascending arch of the aorta, which had ruptured in two places through the anterior thoracic walls, died suddenly after repeated copious hemorrhages from the aneurism, but not immediately after the loss of blood. The autopsy was made in cool weather *eight hours after death* while the body was still warm, there being no odor or evidence of ordinary cadaveric decomposition present. The heart and blood-vessels everywhere were found to contain gas-bubbles in large amount; gas was also present in the subcutaneous connective tissue in some places, in the heart-muscle, liver and other organs. There was a solution of the blood coloring matter evidenced by the color of the blood, the diffuse red staining of the inner coat of the vessels and of the tissues in the pelvis of the kidney. The bacterioscopic examination of the blood revealed the presence of non-motile, capsulated bacilli in very large number wherever gas was found, and no other species of micro-organism could be detected. This bacillus was isolated in pure culture and found to be an obligatory anaerobe. Its morphological and biological properties were studied and have been described. An exact reproduction in every particular of the condition in the body relating to the presence of gas and changes caused by the bacillus was obtained by the injection of pure cultures of the bacillus into the circulation of rabbits shortly before killing the animal. No accurate determination of the gases produced by the growth of the bacillus was made save to establish by ignition the presence of hydrogen both in the original case and in the experimental animals.

There can be no doubt that the gas found in the vessels and organs at the autopsy on the patient was not atmospheric air, but was produced by the growth of the bacilli. The questions which at once suggest themselves are: Were these bacilli distributed throughout the circulation before the death of the patient? At what point did they enter the circulation? Were they concerned in causing death? An unequivocal answer cannot be given to these questions.

As regards the first question, the experiments upon animals



speak strongly in favor of the view that the bacilli had entered the circulation before death. When these bacilli were introduced into the heart of the rabbit after death, it required so much longer for them to spread throughout the vessels and organs with gas formation as compared with their development when the bacilli were previously carried throughout the body by the circulation, that it seems doubtful that in the short space of eight hours, the body being kept in a cool place, the bacilli starting at one point could have developed so extensively and have produced so much gas throughout the vessels and organs as were found at the autopsy on the patient. Even when the animal was kept from the time of death at a temperature of 32° C. the bacilli which had been introduced after death into the right ventricle had not made their appearance in the abdominal aorta or the peripheral veins or produced gas-blebs in the liver after 7½ hours (experiment 7). On the other hand we have experimental evidence of quite as rapid post-mortem development of bacilli and gas as that occurring in the patient J. M. when the organisms have been previously introduced into the circulation. It may, however, be urged that special conditions favoring the growth of the bacilli, such as the disappearance of oxygen and possibly of other restraining influences of the fluids and cells, may have appeared in the anæmic body of the tuberculous patient at an earlier period after death than they do in the previously healthy animal.

Regarding the point of entrance of the bacilli it seems to us probable that they entered the aneurismal sac through the external openings in the chest wall. The sac of the large aneurism was nearly filled with laminated ante-mortem coagula. The conditions would seem to be suitable for the development of the bacilli in this thick clot, in the deeper parts of which we may suppose the oxygen to be in so small an amount as to permit the growth of the bacillus. The excellent development of the organism in fluid cultures with Buchner's method of anaerobic culture before there has been time for complete absorption of the oxygen, and the height to which it grows in solid agar cultures, indicate that it is not so susceptible to the restraining influence of a small amount of oxygen as are some strictly anaerobic organisms, and we believe therefore that it could find conditions for its growth in the thick clot of the aneurism, which was virtually shut off from the circulation, as well as in high layers of gelatine and agar

exposed to the air. The aneurismal clot was found at the autopsy to be riddled with gas and discolored around the gas and to contain in enormous number the bacilli, in apparently pure culture. There was no other place in the body where equally favorable conditions for the growth of the organism were present unless it be in the intestinal canal, and the possibility of the entrance of the bacilli from the latter source cannot be absolutely excluded.

If, as seems quite possible, the bacilli had entered through the ulcerated openings the clots of the aneurism and effected growth there before death, then the conditions seem to have been such as to permit the escape of gas into the circulation during life, the bacilli being also carried in just as they are carried to the surface of agar cultures by the escaping gas. The reduction of the blood pressure by the extremely exhausted and anæmic state of the patient would be a factor favoring the escape of the gas into the circulation. The splitting and elevation of masses of agar in our cultures show that the developing gas is capable of exerting considerable pressure. It seems to us therefore by no means impossible that the entrance of gas and of bacilli into the circulation from the aneurism may have been concerned in the death of the patient, which, as already stated, was sudden. Nevertheless we would express ourselves with reserve on these points. There were present other conditions sufficient to cause death, even sudden death; but in the light of experiments upon animals, all of the circumstances of the case seem best explained upon the supposition that the bacilli had begun to grow in the aneurismal clot and were carried into the circulation before death.

The experiments upon animals show that the bacilli are incapable of development in the circulating blood during life, as might have been predicted from the anaerobic character of the organism. If, however, the bacilli should find access to dead tissue, old fibrinous clots, cavities such as the intestine or uterus, under conditions where the amount of free oxygen is reduced to a minimum, there they might grow; and if the places where they develop communicate with the circulatory channels, then the gas produced and with it the bacilli might enter the circulation.

As is well known a large number of cases have been reported during the last seventy years of death in human beings attributed to the entrance of air into the veins, and a large amount

of experimental work has been done both before and since this period in regard to the effects of the entrance of air into the circulation.

The experiments have shown that the sudden introduction of a large amount of air into the veins of rabbits and dogs is fatal, the lethal quantity for dogs when rapidly injected into the jugular vein varying according to Nysten<sup>1</sup> from 40 to 120 cc., according to the size of the dog. Smaller quantities than this have, however, proved fatal to dogs. Hare,<sup>2</sup> who also found that quantities short of 40 cc. did not kill dogs, believes that no such amount of air as would cause death in human beings can enter a vein injured by the surgeon's knife. While it is true that many of the cases reported as deaths due to entrance of air into veins opened by the surgeon are unsupported by any satisfactory evidence that this was the cause of death, still we cannot agree with Hare that all of the reported cases are of this character. The evidence seems to us conclusive in some of the cases that death really resulted from the sudden entrance of air.

When the air is introduced slowly and at intervals, enormous quantities can be injected in a comparatively short time without manifest injury. Thus Laborde and Muron<sup>3</sup> injected into the external jugular vein of a dog 1120 cc. in the space of one hour and a half without causing death, and Jürgensen<sup>4</sup> injected into the left femoral artery of a narcotized dog weighing 43.5 kilo. 3650 cc. in the space of two hours and twenty-five minutes with only slight disturbance of the respiration and of the action of the heart. Under these circumstances the air-bubbles pass through the capillaries and circulate with the blood, but of course with such enormous quantities much of the air must be speedily eliminated.

The reported cases in human beings in which death has been attributed to the entrance of air into the circulation may be brought for the most part, although not wholly, into the following classes: surgical operations, especially about the neck, shoulder and skull; cases in which the air has entered

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<sup>1</sup> Nysten. *Recherches de physiologie et de chimie pathologiques*. Paris, 1811.

<sup>2</sup> Hare. *Therapeutic Gazette*, Sept. 16, 1889.

<sup>3</sup> Laborde and Muron. *Comptes rendus de la Soc. de Biologie*, 1873, t. V.

<sup>4</sup> Jürgensen. *Deutsches Archiv f. klin. Med.*, Bd. 31, p. 458, 1882.

the uterine veins, chiefly from the puerperal uterus, either spontaneously as after attempted abortions, or after injections into the uterine cavity; cases in which the air has entered from the stomach or intestine, and cases in which no point of entrance for the air could be detected.

We have already expressed our belief in the credibility of some in the first class of cases. We see also no reason to question a similar interpretation of such a case as that reported by Vogel,<sup>1</sup> in which a caseous lymphatic gland had brought about a communication between the right subclavian vein and a large bronchus. Death was instantaneous, and at the autopsy large air-bubbles were found in the blood and in different abdominal organs.

The evidence is also strongly in favor of the view that some of the sudden deaths in the puerperal state which have been attributed to the entrance of air into the uterine sinuses, especially after injections of fluid and air into the cavity of the uterus, are in fact due to the assigned cause.

In 1882 Jürgensen<sup>2</sup> reported a case of sudden death of a patient with gastric ulcer which had bled profusely shortly before death. At the autopsy 22 hours after death gas was found in the blood-vessels, the peritoneal cavity, the pericardial sac, the sub-peritoneal tissue, the spleen and the liver, which was emphysematous. In the floor of the ulcer, which had not perforated into the peritoneal cavity, was found an open vein, probably the splenic, 3 to 4 mm. in diameter. Jürgensen believes that the air found post-mortem in the vessels entered the circulation during life through the open vein in the floor of the ulcer, passed through the portal capillaries into the hepatic veins to the inferior vena cava and the right heart, thence through the pulmonary circulation to the left heart and the systemic circulation. This interpretation seems to us altogether improbable, and one of us<sup>3</sup> in 1885 suggested that in this case the gas developed in the vessels after death, attention being called to the presence of gas elsewhere than in the blood-vessels in this case, a point which Jürgensen does not consider in his first report. In 1887 Jürgensen<sup>4</sup> reported

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<sup>1</sup> Vogel. *Berliner klin. Wochenschrift*, 1882, No. 12.

<sup>2</sup> Jürgensen, *loc. cit.*

<sup>3</sup> Welch. *A System of Practical Medicine by American Authors*, edited by William Pepper. Vol. II., p. 510. Philadelphia, 1885.

<sup>4</sup> Jürgensen. *Deutsches Archiv f. klin. Med.*, Bd. 41, p. 569, 1887.

another case occurring a few months after the first, in which a gastric ulcer had perforated into the peritoneal cavity. At the autopsy, 22 hours after death, gas was found in the peritoneal and pleural cavities, the heart, arteries and veins, and the subcutaneous tissues of the abdomen. There was beginning green discoloration of the abdominal walls. No vessels with ulcerated openings were found in the ulcer or elsewhere. This case is interpreted by Jürgensen in an entirely different manner from the first, the gas in the vessels as well as that in the serous cavities and connective tissue being attributed to a gas-generating something, presumably a microbe, but he thinks the gas was developed in the circulation partly during life because just before death the jugular veins on the right side of the neck were observed to swell up, a phenomenon noted also in the first case. In the light of our case and of the investigations reported in this article these cases are open to a clear and satisfactory interpretation without recourse to the adventurous hypothesis advanced by Jürgensen in his first article.

A considerable number of cases are to be found in medical literature in which gas, which could not be explained as due to ordinary cadaveric decomposition, was found in the blood-vessels after death, without any opening through which air could enter the circulation. In some the death was sudden, and no satisfactory cause of death could be found except the gas in the blood. Some of these cases are very curious, as will be seen by those who consult the works of Cless<sup>1</sup> and of Couty.<sup>2</sup> Most writers dismiss these cases as unworthy of credence, or as referable to ordinary post-mortem decomposition, or as attributable to the entrance of air during the post-mortem examination. Some of the older writers and even modern ones have seriously discussed the possibility of the spontaneous generation of air or gas in the circulating blood during life as an explanation of these cases. Ewald and Kobert<sup>3</sup> believe that they have found the key to their solution by their demonstration that the lungs during life are not airtight, but apparently without rupture permit under pressure air

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<sup>1</sup> Cless. *Luft im Blute*. Stuttgart, 1854.

<sup>2</sup> Couty. *Etude expérimentale sur l'entrée de l'air dans les veines et les gas intravasculaires*. Thèse, Paris, 1875.

<sup>3</sup> Ewald and Kobert. *Pflüger's Archiv f. d. gesammte Physiologie*, 1883, Bd. 31, p. 182.



to be forced through which makes its appearance in the pleural cavities and in the blood of the heart and elsewhere. Our observations reported in this article suggest an explanation of some of these cases more satisfactory than those hitherto offered.

Fischer,<sup>1</sup> in his well-known paper on the dangers of the entrance of air into the veins, justly says: "The weakest part of the entire doctrine regarding the entrance of air into the veins of human beings during an operation is the extremely variable and undemonstrative character of the recorded autopsies." Although he does not say so, he evidently quotes from Greene's article,<sup>2</sup> which is the best consideration of the literature of the subject which has come to our notice in the English language up to the date of its publication (1864), in giving the number of autopsies as only eighteen and in stating that in only six of these is there any statement as to the length of time between death and the post-mortem examination, in five of these cases the time being 18 to 26 hours and in one 52 hours.

May reports a case of sudden death in the puerperal state in which the autopsy was made 6 hours after death, and in which he considers that the presence of air in the vessels was the only cause to which death could be attributed.<sup>3</sup> At the other extreme is a case for which the same explanation is accepted and in which the vessels were examined for the presence of gas five days after death.

Any one who will examine with a critical spirit the reported cases of death from the entrance of air into the vessels will be impressed with the unsatisfactory and meagre evidence upon which this conclusion as to the cause of death is based in the majority of the cases. In some of the cases the gas found in the vessels was associated with the most ordinary advanced post-mortem decomposition, which, as is well known, in some conditions may set in with great rapidity. Had there been no bacteriological examination in our case, the evidence in support of the view that air had entered the vessels during life would have been indeed stronger than in most of the reported cases. The patient had been weakened by copious hemorrhage, which in the writings on the subject is regarded as an important predisposing factor. A communication existed between

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<sup>1</sup> Fischer. Volkmann's Sammlung klin. Vorträge, No. 113.

<sup>2</sup> Greene. Am. Journ. Med. Sciences, 1864, Vol. 47, p. 38.

<sup>3</sup> May. Trans. Path. Soc. London, 1858, Vol. IX., p. 158.

the external air and an intra-thoracic vessel. Death was sudden. The autopsy, made in cool weather eight hours after death without the slightest visible sign or odor of post-mortem decomposition, revealed gas in large quantity in the vessels.

We have not been able to find any report of a bacteriological examination of the blood in the cases in which gas supposed to be air entering during life has been found in the vessels after death, and it is certainly surprising that no attempt has been made to determine by bacteriological examination whether or not what was taken to be atmospheric air might not be generated by the growth of a micro-organism. The result of the examination in our case must necessarily cast doubt upon the interpretation hitherto accepted in many of the cases reported as death due to the entrance of air into the veins. A principal link in the chain of evidence has fallen out, viz., the belief that when the gas is found in the heart and vessels a few hours after death without any evidence of cadaveric decomposition, this is a proof that the gas is air, and is not the result of the development of a micro-organism. Hereafter in all similar cases a careful bacteriological examination, including anaerobic cultures, must be made before it can be admitted that the gas in the vessels has not been generated by micro-organisms. Time only can determine whether such examinations will show that the explanation found to be correct in our case is exceptional or is applicable to many other cases which might otherwise be interpreted as due to the entrance of air into the vessels.





















